AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph on page 2, beginning at line 9 and ending at line 14, with the following amended paragraph:

The present invention provides a novel member of the Bin1/Amphiphysin/RVS (BAR) proteins, termed herein Bin2. Bin2 proteins, nucleic acids, and other Bin2 compositions of the invention have a variety of uses related to regulation of cell growth control, cell survival, differentiation, endocytosis and actin organization, as well as for the diagnosis and treatment of conditions associated with aberrant cell behavior.

Please replace the paragraph on page 5, beginning at line 1 and ending at line 5, with the following amended paragraph:

In a further aspect, the invention provides a method of detecting inappropriate expression of Box-dependent myc-interacting peptide-2 ~~(Bin 2)~~(Bin2) in a patient comprising providing a sample from a patent suspected of having said inappropriate expression and performing nucleic acid amplification using a Bin2 nucleic acid sequence of the invention.

Please replace the paragraph on page 12, beginning at line 3 and ending at line 27, with the following amended paragraph:

As known in the art, "homology" or "identity" means the degree of sequence relatedness between two peptide or two nucleotide sequences as determined by the identity of the match between two lengths of such sequences. Both identity and homology can be readily calculated by methods extant in the prior art [See, e.g., COMPUTATIONAL MOLECULAR BIOLOGY, Lesk, A.M., ed., Oxford University Press, New York, (1988); BIOCOMPUTING: INFORMATICS AND GENOME PROJECTS, Smith, D.W., ed., Academic Press, New York, (1993); COMPUTER ANALYSIS OF SEQUENCE DATA, PART I, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, (1994); SEQUENCE ANALYSIS IN MOLECULAR BIOLOGY, von Heinje, G., Academic Press, (1987); and SEQUENCE ANALYSIS PRIMER, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, (1991)].

While there exist a number of methods to measure identity and homology between two nucleotide sequences, the terms "identity", "similarity" and ~~homology~~"homology" are well known to skilled artisans [H. Carillo and D. Lipton, *SIAM J. Applied Math.*, **48**:1073 (1988)]. Methods commonly employed to determine identity or homology between two sequences include, but are not limited to, those disclosed in GUIDE TO HUGE COMPUTERS, Martin J. Bishop, ed., Academic Press, San Diego, 1994. Preferred methods to determine identity or homology are designed to give the largest match between the two sequences tested. Methods to determine identity and similarity are codified in computer programs. Preferred computer program methods to determine identity and homology between two sequences include, but are not limited to, the algorithm BESTFIT from the GCG program package [J. Devereux *et al., Nucl. Acids Res.*, **12**(1):387 (1984)], the related MACVECTOR program (Oxford), and the FASTA (Pearson) programs, which may be used at default settings or modified settings such as determined to be suitable by one of skill in the art.

Please replace the paragraph beginning on page 12, line 28, and ending on page 13, line 13, with the following amended paragraph:

A Bin2 peptide or protein of the present invention may also be modified to increase its ability to bind and thus, complex with, Bin1. For example, the Bin2 peptide or protein may be coupled to [[a]]chemical compounds or non-proteinaceous carriers. In certain embodiments, the coupling is designed not to interfere with the desired biological activity of either the Bin2 peptide or protein or the carrier. For a review of some general considerations in coupling strategies, see Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory, ed. E. Harlow and D. Lane (1988). For example, the carrier may be selected which facilitates cell penetration, e.g. a lipid or a carbohydrate. As another example, the carrier may be selected to deliver a toxin to Bin1, to which the Bin2 peptide binds. Such toxins are known to those of skill in the art and may include, e.g., chemical compounds including, without limitation, dinitrophenol groups and arsonilic acid. Yet other carriers may be selected simply to facilitate production or delivery of the Bin2 peptide or protein. For example, useful carriers known in the art, include, without

limitation, keyhole limpet hemocyanin (KLH); bovine serum albumin (BSA), ovalbumin, agarose beads; activated carbon; or bentonite.

Please replace the paragraph on page 14, beginning on line 11 and ending on line 13, with the following amended paragraph:

In yet another example, a Bin2 fragment may be a T cell epitope. Such a T cell epitope ~~may be readily identified~~ may be readily identified using available computer ~~modelling~~modeling programs.

Please replace the paragraph on page 14, beginning on line 23 and ending on line 25, with the following amended paragraph:

The Bin2 peptides and ~~protein~~proteins of the present invention, or fragments of ~~it~~them, may also be constructed, using conventional genetic engineering techniques as part of a larger and/or multimeric protein or protein ~~compositions~~composition.

Please replace the paragraph beginning on page 14, line 26, and ending on page 15, line 2, with the following amended paragraph:

For example, such a fusion protein may be desirable in order to improve yield on expression and/or purification. Suitable fusion partners for such a purpose are well known to those of skill in the art and include, e.g., ~~glutatione-S-transferase~~glutathione-S-transferase and maltose binding protein. Alternatively, a fusion protein of the invention may be composed of a Bin2 fragment, such as a fragment corresponding to a T cell epitope or to the Bin1 binding region, which is fused to an active agent.

Please replace the paragraph on page 17, beginning on line 5 and ending on line 13, with the following amended paragraph:

~~Similarly~~Similarly, bacterial cells are useful as host cells for the present invention. For example, the various strains of *E. coli* (e.g., HB101, MC1061, and strains used in the following examples) are well-known as host cells in the field of biotechnology. Various strains of *B. subtilis*, *Pseudomonas*, other bacilli and the like

may also be employed in this method. Many strains of yeast cells known to those skilled in the art are also available as host cells for expression of the polypeptides of the present invention. Other fungal cells may also be employed as expression systems. Alternatively, insect cells such as *Spodoptera frugipedera* (Sf9) cells may be used, e.g., in the baculovirus expression system.

Please replace the paragraph on page 19, beginning on line 10 and ending on line 20, with the following amended paragraph:

Further provided by the present invention are anti-idiotype antibodies (Ab2) and anti-anti-idiotype antibodies (Ab3). Ab2 are specific for the target to which anti-Bin2 antibodies of the invention bind and Ab3 are similar to Bin2 antibodies (Ab1) in their binding specificities and biological activities [see, e.g., M. Wettendorff *et al.*, "Modulation of anti-tumor immunity by anti-idiotypic antibodies." In IDIOTYPIC NETWORK AND DISEASES, ed. by J. Cerny and J. Hiernaux J, Am. Soc. Microbiol., Washington DC: pp. 203-229, (1990)]. These anti-idiotype and anti-anti-idiotype antibodies may be produced using techniques well known to those of skill in the art. Such anti-idiotype antibodies (Ab2) can bear the internal image of [[the]]Bin1 and bind to it in much the same manner as Bin2 and are thus useful for the same purposes as Bin2.

Please replace the paragraph on page 19, beginning on line 21 and ending on line 30, with the following amended paragraph:

In general, polyclonal antisera, monoclonal antibodies and other antibodies which bind to Bin2 as the antigen (Ab1) are useful to identify epitopes of Bin2, to separate Bin2 from contaminants in living tissue (e.g., in chromatographic columns and the like), and in general as research tools and as starting material essential for the development of other types of antibodies described above. Anti-idiotype antibodies (Ab2) are useful for binding Bin2 and thus may be used in the treatment of cancers in which Bin2 is part of a biochemical cascade of events leading to carcinoma. The Ab3 antibodies may be useful for the same reason the Ab1 are useful. Other uses as research tools and as components for separation of Bin2 from other ~~contaminant~~contaminants of living tissue, for example, are also contemplated for these antibodies.

Please replace the paragraph on beginning on page 34, line 24, and ending on page 35, line 7, with the following amended paragraph:

Northern analyses of total RNAs isolated from human tissues and cell lines [[was]]were performed using the Bin2 cDNA as a hybridization probe to investigate the range of expression of Bin2 and to compare it with amphiphysin and Bin1 expression. Prior to Northern analysis, cells were treated with DMSO or RA for 1, 3 or 5 days and RNA was isolated for Northern analysis with Bin2 cDNA. The human tissues studied included heart, brain, placenta, lung, liver, skeletal muscle, kidney, pancreas, spleen, thymus, prostate, testis, ovary, small intestine, colon, and peripheral blood leukocytes. The cell lines included: Raji, 380, 697, VM173, GM1500, ALL200, Daudi, HepG2, Caco-2, HCT116, LoVo, HBL100, ZR75-1, MCF7, BT20, SK-BR-3, A549, HLF, DU145, LNCaP, PC3, U373, U87-MG, and NCH2. Also determined was the level of Bin2 induction during differentiation of HL60 promyelocytic leukemia cells to monocytes.

Please replace the paragraph on page 38, beginning on line 8 and ending on line 22, with the following amended paragraph:

Bin1 and Bin2 were shown to form a stable biochemical complex, in the manner of RVS161 and RVS167 in yeast or amphiphysin and neuronal splice isoforms of Bin1 in mammalian cells [Navarro *et al.,* cited above (1997); Wigge *et al.,* cited above (1997)], and the association depended upon the integrity of the BAR domain. Bin2 did not affect the tumor suppressor properties of Bin1 that are manifested in HepG2 cells [Sakamuro *et al., Nature Genet.* **14:** 69-77 (1996)]. This may reflect different requirements for each activity, since Bin2 association rested on an N-terminal BAR determinant whereas the tumor suppressor activity of Bin1 rests upon a C-terminal BAR determinant. Evidence that BAR domains encode unique activities [[an]]and are not functionally equivalent is provided by domain swapping studies performed in yeast [Sivadon *et al., FEBS Lett.* **417:** 21-27 (1997)]. Thus, the BAR domain of Bin2 may have unique features, perhaps related to Bin1 regulation rather than effector signaling. In future work, it will be important to determine the physiological functions of Bin2 and how they are manifested independently or in an integrated manner with the functions of Bin1.